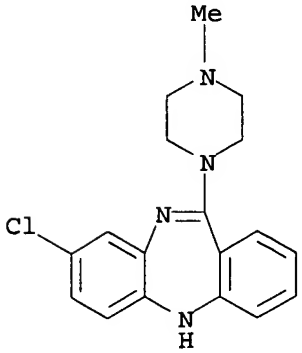
L19 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:818663 CAPLUS
DOCUMENT NUMBER: 138:150503
TITLE: Functional characterization of alternatively spliced 5-HT2 receptor isoforms from the pharynx and muscle of the parasitic nematode, Ascaris suum
AUTHOR(S): Huang, Xinyan; Xiao, Hong; Rex, Elizabeth B.; Hobson, Robert J.; Messer, William S., Jr.; Komuniecki, Patricia R.; Komuniecki, Richard W.
CORPORATE SOURCE: Department of Biological Sciences, University of Toledo, Toledo, OH, 43606, USA
SOURCE: Journal of Neurochemistry (2002), 83(2), 249-258
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serotonin (5-HT) receptors play key regulatory roles in nematodes and alternatively spliced 5-HT2 receptor isoforms have been identified in the parasitic nematode, A. suum. 5-HT2As1 and 5-HT2As2 contain different C-termini, and 5-HT2As1Δ4 lacks 42 amino acids at the C-terminus of the 3rd intracellular loop. 5-HT2As1 and 5-HT2As2 exhibited identical pharmacol. profiles when stably expressed in human embryonic kidney (HEK) 293 cells. Both 5-HT2As isoforms had higher affinity for 5-HT than their closely related Caenorhabditis elegans homolog (5-HT2Ce). This increased 5-HT affinity was not related to the substitution in 5-HT2As1 of F120 for Y in the highly conserved DRY motif found in the 2nd intracellular loop of other 5-HT receptors, since a 5-HT2As1F120Y mutant actually exhibited increased 5-HT affinity compared with that of 5-HT2As1. As predicted, cells expressing either 5-HT2As1 or 5-HT2As2 exhibited a 5-HT-dependent increase in phosphatidylinositol (PI) turnover. In contrast, although 5-HT2As1Δ4 displayed a 10-fold higher affinity for 5-HT and 5-HT agonists than either 5-HT2As1 or 5-HT2As2, 5-HT2As1Δ4 did not couple to either PI turnover or adenyl cyclase activity. Based on RT-PCR, 5-HT2As1 and 5-HT2As2 were more highly expressed in pharynx and body wall muscle and 5-HT2As1Δ4 in nerve cord/hypodermis. This is the 1st report of different alternatively spliced 5-HT2 receptor isoforms from any system.

IT **5786-21-0**, Clozapine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(alternatively spliced 5-HT2 receptor sequence and functional characterization in pharynx and muscle of parasitic **nematode**)

RN 5786-21-0 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

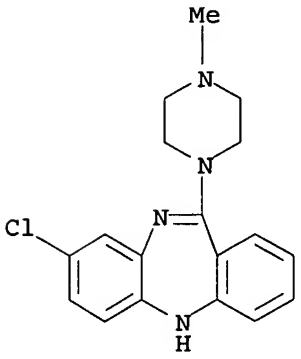


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:214705 CAPLUS
DOCUMENT NUMBER: 130:335480
TITLE: Characterization of a novel serotonin receptor from Caenorhabditis elegans: cloning and expression of two splice variants
AUTHOR(S): Hamdan, Fadi F.; Ungrin, Mark D.; Abramovitz, Mark; Ribeiro, Paula
CORPORATE SOURCE: Institute of Parasitology, McGill University, Ste. Anne de Bellevue, QC, H9X 3V9, Can.
SOURCE: Journal of Neurochemistry (1999), 72(4), 1372-1383
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have cloned a novel receptor cDNA from C. elegans (5-HT2Ce) that has high sequence homol. with 5-HT2 receptors from other species. When transiently expressed in COS-7 cells, 5-HT2Ce exhibited 5-HT binding activity and activated Ca2+-mediated signaling in a manner analogous to other 5-HT2 receptors. However, 5-HT2Ce displayed unusual pharmacol. properties, which resembled both 5-HT2 and 5-HT1-like receptors but did not correlate well with any of the known 5-HT2 subtypes. Two splice variants of 5-HT2Ce that differ by 48 N-terminal amino acids were identified. The 2 isoforms were found to have virtually identical binding and signaling properties but differed in their levels of mRNA expression, with the longer variant being 4-fold more abundant than the shorter species in all developmental stages tested. Taken together, the results describe 2 variants of a novel C. elegans 5-HT receptor, which has some of the properties of the 5-HT2 family but whose pharmacol. profile does not conform to any known class of receptor.

IT **5786-21-0**, Clozapine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cloning and expression of two splice variants of a novel serotonin receptor from **nematodes**)
RN 5786-21-0 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:420905 CAPLUS
DOCUMENT NUMBER: 101:20905
TITLE: Efferent neurotransmission of circadian rhythms in Limulus lateral eye. I. Octopamine-induced increases

in retinal sensitivity

AUTHOR(S): Kass, Leonard; Barlow, Robert B., Jr.

CORPORATE SOURCE: Inst. Sens. Res., Syracuse Univ., Syracuse, NY, 13210, USA

SOURCE: Journal of Neuroscience (1984), 4(4), 908-17
CODEN: JNRSDS; ISSN: 0270-6474

DOCUMENT TYPE: Journal

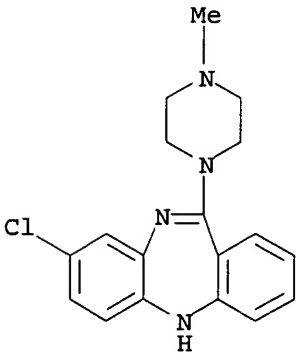
LANGUAGE: English

AB Octopamine increases the sensitivity of the Limulus lateral eye in situ when injected beneath the cornea during the day. The effect of octopamine is dose-dependent with a threshold concentration of about 0.1 μM injected at 1 μL/min for 15 min. Injection of 40 μM octopamine increases lateral eye sensitivity to approx. 70% of the nighttime level normally caused by the efferent output of a circadian clock. Injections of octopamine analogs and other candidate neurotransmitters indicate that the postsynaptic receptor mediating the increase of retinal sensitivity is relatively specific for the structure of octopamine. The postsynaptic receptor is tentatively classified as a type 2B octopamine receptor. Clozapine suppresses the effects of both exogenous octopamine and the endogenous efferent neurotransmitter. These and previous results indicate that retinal efferents, driven by a circadian clock in Limulus brain, release octopamine that increases visual sensitivity.

IT **5786-21-0**
RL: BIOL (Biological study)
(octopamine-induced enhancement of photosensitivity of lateral eye of **arthropod** inhibition by)

RN 5786-21-0 CAPLUS

CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



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L32 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:804461 CAPLUS
DOCUMENT NUMBER: 123:198834
TITLE: N-Heterobicyclyl-piperazinyl or -piperidinyl tricyclic derivatives useful as dopamine receptor ligands
INVENTOR(S): Tehim, Ashok; Fu, Jian-Min; Rakhit, Sumanas
PATENT ASSIGNEE(S): Allelix Biopharmaceuticals Inc., Can.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9517400	A1	19950629	WO 1994-CA687	19941214
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2179306	AA	19950629	CA 1994-2179306	19941214
CA 2179306	C	20001107		
AU 9511899	A1	19950710	AU 1995-11899	19941214
EP 736024	A1	19961009	EP 1995-902734	19941214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09506868	T2	19970708	JP 1994-517063	19941214

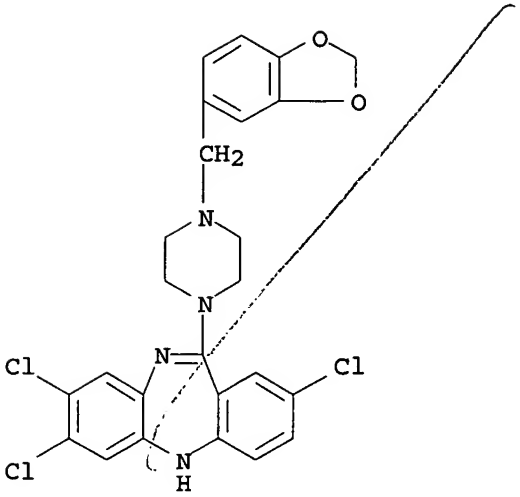
PRIORITY APPLN. INFO.: US 1993-172208 A 19931223
WO 1994-CA687 W 19941214

OTHER SOURCE(S): CASREACT 123:198834; MARPAT 123:198834

AB Dopamine D4 receptor-selective compds. are disclosed, specifically I [rings A, B = (un)substituted, (un)saturated 5- or 6-membered, homo- or heterocyclic rings; X1 = CH2, O, NH, S, CO, CH(OH), CH[CH(C1-4-alkyl)2], C:CHCl, C:CHCN, N(C1-4-alkyl), NAc, SO2, SO; X2 = N:, CH2CH:, CO, O, S; R1 = C1-4 alkyl; Y = CH, N; n = 0-2; q = 1-2; R2 = C1-6 alkyl bridge optionally incorporating N, O and S; ring D = cyclohexane or benzene nucleus; ring E = (un)saturated 5- or 6-membered heterocycle incorporating 1-3 of O, N, and/or S and (un)substituted by 1-2 of halo, C1-4 alkyl, haloalkyl] and their acid addition salts, solvates, and hydrates. Their uses as ligands for dopamine receptor identification, in a drug screening program, and as pharmaceuticals for, e.g., schizophrenia, are also described. Eighteen compds. I were claimed, prepared, and/or tested. Various salts and precursors were also prepared For example, condensation of 8-chlorodibenz[b,f][1,4]oxazepin-11(10H)-one [preparation briefly described] with 1-piperonylpiperazine in refluxing PhMe in the presence of TiCl4 gave title compound II. As the most preferred embodiment of the invention, II exhibited better D4 affinity and selectivity than the standard D4 antagonist clozapine. For example, II had D4 receptor Ki of 4, vs. 23 for clozapine, and a D2/D4 ratio of 23.8, vs. 10 for clozapine.

IT **167996-86-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinyl and piperidinyl tricyclics as dopamine receptor ligands)

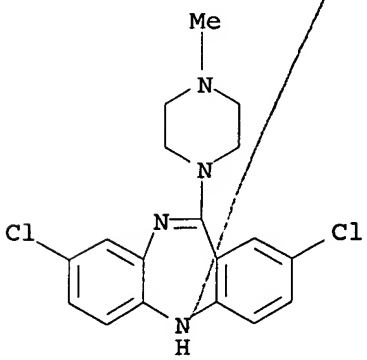
RN 167996-86-3 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 11-[4-(1,3-benzodioxol-5-ylmethyl)-1-piperazinyl]-2,7,8-trichloro- (9CI) (CA INDEX NAME)



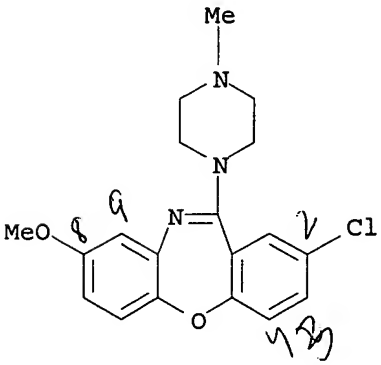
L32 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:400178 CAPLUS
DOCUMENT NUMBER: 105:178
TITLE: Analysis of the pharmacological properties of clozapine analogs using molecular electrostatic potential surfaces
AUTHOR(S): Weber, H. P.; Lybrand, T.; Singh, U.; Kollman, P.
CORPORATE SOURCE: Sch. Pharm., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Journal of Molecular Graphics (1986), 4(1), 56-60, 38 CODEN: JMGRDV; ISSN: 0263-7855
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mol. electrostatic potential surfaces were used to study a series of neuroleptic compds., clozapine [5786-21-0] and clozapine analogs, with similar structures but two rather different pharmacol. profiles. Using the electrostatic potential surfaces, the compds. studies could be assigned to one of two distinct categories corresponding to the two pharmacol. classes. The results suggest that the mol. electrostatic potential surfaces may be useful in the a priori prediction of pharmacol. properties of untested clozapine analogs.

IT **55051-40-6**
RL: PRP (Properties)
(anticholinergic activity and extrapyramidal side effects of, structure in relation to)
RN 55051-40-6 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

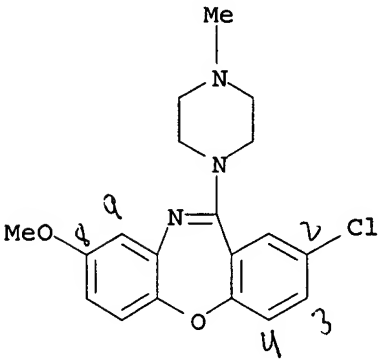


L32 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:483331 CAPLUS
DOCUMENT NUMBER: 99:83331
TITLE: Applications of capillary gas chromatography in routine toxicological analyses
AUTHOR(S): Anderson, W. H.; Stafford, D. T.
CORPORATE SOURCE: Cent. Health Sci., Univ. Tennessee, Memphis, TN, 38163, USA
SOURCE: HRC & CC, Journal of High Resolution Chromatography and Chromatography Communications (1983), 6(5), 247-54
CODEN: HCJCDB; ISSN: 0344-7138
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Drug screening via gas chromatog., fused silica capillary columns coated with a 0.25 μm film of SE 30, yielded retention indexes which were reproducible to within 4 units of library values. Screening was performed on a temperature programmed column at 100°-295° at 5°/min with He carrier velocity of 45 cm/s at 100°. The retention index system of E. Kovats (1958) was used to characterize the drugs via linear interpolation between adjacent hydrocarbons. The retention indexes of 175 basis drugs are given. The capillary column provides superior resolution and/or greatly reduced anal. time relative to packed columns and is thus well suited to emergency toxicol. situations in forensic labs.
IT **70020-54-1**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, by gas chromatog. on capillary columns, legal chemical in relation to)
RN 70020-54-1 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 2-chloro-8-methoxy-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L32 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:203363 CAPLUS
DOCUMENT NUMBER: 94:203363
TITLE: Postmortem blood and tissue levels of loxapine and its metabolites
AUTHOR(S): Cooper, T. B.; Bost, R.; Sunshine, I.
CORPORATE SOURCE: Rockland Res. Inst., Orangeburg, NY, 10962, USA
SOURCE: Journal of Analytical Toxicology (1981), 5(2), 99-100
CODEN: JATOD3; ISSN: 0146-4760
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Loxapine (I) [1977-10-2] and its metabolites were extracted from the blood and tissue specimens obtained at autopsy and analyzed by gas chromatog. Tissue distributions of I and its metabolites are presented.
IT **70020-54-1**
RL: ANT (Analyte); ANST (Analytical study)

(determination of, in postmortem blood and tissues by gas chromatog.)
RN 70020-54-1 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 2-chloro-8-methoxy-11-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



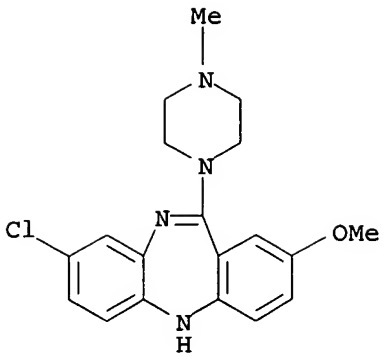
L32 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:568316 CAPLUS
DOCUMENT NUMBER: 93:168316
TITLE: Procataleptogenic 5H-dibenzo[b,e]-1,4-diazepine derivative
INVENTOR(S): Protiva, Miroslav; Sindelar, Karel; Dlabac, Antonin
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 3 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 179793	B	19770331	CS 1976-969	19760213

PRIORITY APPLN. INFO.: CS 1976-969 19760213

AB The title compound I did not have cataleptic activity but it potentiated the cataleptic activity of other neuroleptics (perphenazine) (LD and ED given). I was prepared by the following route: a mixture of HCl salt of 5-aminoanthranilic acid, 2,5-Cl2C6H3NO2, K2CO3, Cu, and HCONMe2 was refluxed and gave N-(4-chloro-2-nitrophenyl)-5-methoxyanthranilic acid. Reduction with Na2S2O4 in a solution of NH4OH gave N-(2-amino-4-chlorophenyl)-5-methoxyanthranilic acid, which was cyclized by refluxing in xylene to 8-chloro-2-methoxydibenzo[b,e]-1,4-diazepin-11[5H,10H]-one. Reaction of this compound with 1-methylpiperazine in a mixture of PhMe and PhOMe in the presence of TiCl4 gave 8-chloro-2-methoxy-11-(4-methylpiperazino)-5H-dibenzo[b,e]-1,4-diazepine. Demethylation with BBr3 in CH2Cl2 gave I.

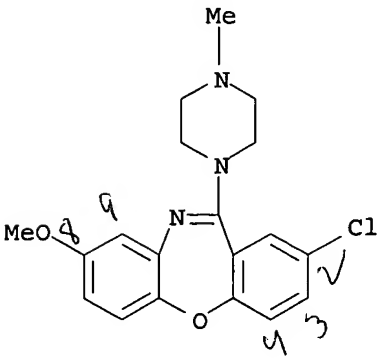
IT **67104-23-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and demethylation of)
RN 67104-23-8 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-2-methoxy-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L32 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:161840 CAPLUS
DOCUMENT NUMBER: 90:161840
TITLE: GLC analysis of loxapine, amoxapine, and their metabolites in serum and urine
AUTHOR(S): Cooper, T. B.; Kelly, R. G.
CORPORATE SOURCE: Rockland Res. Inst., Orangeburg, NY, USA
SOURCE: Journal of Pharmaceutical Sciences (1979), 68(2), 216-19
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A gas chromatog. (glass tubes with 3% SP 2100 on 100-200 mesh Supelcoport; Ar-C2H4 (95:5) or He as carrier gas) anal. is presented for loxapine [1977-10-2], amoxapine [14028-44-5], and their major metabolites in serum and urine. Electron-capture detection was employed for serum anal., and flame ionization for urine anal. The procedure included trifluoroacetylation of secondary amine functions, followed by trimethylsilylation of phenolic groups after Et acetate extraction of the sample. Urine required prior enzymic hydrolysis of conjugates. Data indicating the utility of the procedure in hospitalized patients and normal volunteers are presented.

IT **70020-54-1**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood and urine, by gas chromatog.)
RN 70020-54-1 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 2-chloro-8-methoxy-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L32 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:443361 CAPLUS
DOCUMENT NUMBER: 89:43361

TITLE: Neurotropic and psychotropic agents. Part CXVII. Noncataleptic neuroleptics; 8-chloro-2-hydroxy-11-(4-methylpiperazino)-5H-dibenzo[b,e]-1,4-diazepine as a potential metabolite of clozapine

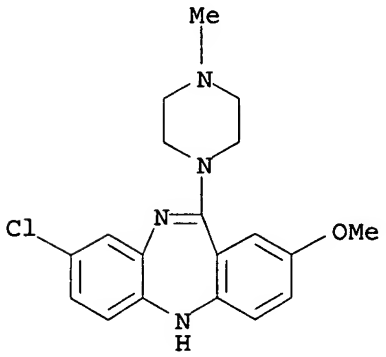
AUTHOR(S): Sindelar, Karel; Dlabac, Antonin; Protiva, Miroslav
CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, Czech.

SOURCE: Collection of Czechoslovak Chemical Communications (1978), 43(1), 309-15
CODEN: CCCCAK; ISSN: 0366-547X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The title compound I was prepared in 5 steps from 2,5-H2N(MeO)C6H3CO2H (II). II was condensed with 2,5-Cl2C6H3NO2 to give N-(4-chloro-2-nitrophenyl)-5-methoxyanthranilic acid which was reduced to the corresponding amino acid and cyclized to 8-chloro-2-methoxydibenzo[b,e]-1,4-diazepin-11(5H,10H)-one (III). Treatment of III with 1-methylpiperazine and TiCl4 gave 8-chloro-2-methoxy-11-(4-methyl-1-piperazinyl)-5H-dibenzo[b,e]-1,4-diazepine which was demethylated with BBr3 in CH2Cl2 to give I. This potential metabolite of clozapine, per se has no cataleptic activity but it potentiates catalepsy produced by perphenazine in rats.

IT **67104-23-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and demethylation of)

RN 67104-23-8 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-2-methoxy-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

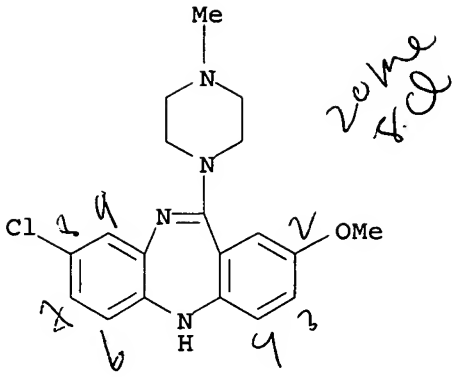


IT **67104-24-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 67104-24-9 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-2-methoxy-11-(4-methyl-1-piperazinyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

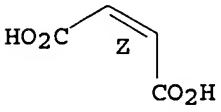
CRN 67104-23-8
CMF C19 H21 Cl N4 O



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

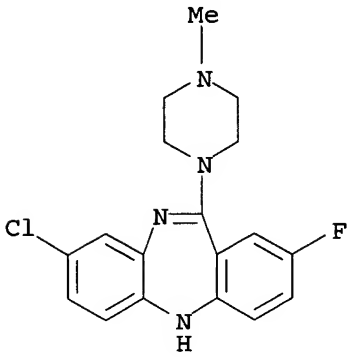


L32 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:593611 CAPLUS
DOCUMENT NUMBER: 87:193611
TITLE: Effects of clozapine and other dibenzo-epines on central dopaminergic and cholinergic systems. Structure-activity relationships
AUTHOR(S): Buerki, H. R.; Sayers, A. C.; Ruch, W.; Asper, H.
CORPORATE SOURCE: Res. Inst. Wander, Wander Ltd., Bern, Switz.
SOURCE: Arzneimittel-Forschung (1977), 27(8), 1561-5
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of halogen substitution in positions R1 and/ or R2 of the piperazinyl dibenzo-epine-hydrochlorides (I, R3 = Me)(X = S, O, NH, or CH2) and the effects of N-hydroxyalkyl substitution in position R3 of clozapine-HCl [54241-01-9](I: X = NH, R1 = Cl, R2 = H, R3 = Me) on locomotor inhibition, cataleptogenesis, apomorphine antagonism, arousal inhibition, striatal dopamine metabolism and on in vivo and in vitro anticholinergic potency were studied in rats. Introduction of Cl into position R2 of I (R1 = H, R3 = Me; X = O or S) resulted in a dramatic increase in extrapyramidal dopaminergic effect, as shown by the emergence of catalepsy and antagonism of apomorphine stereotypies, but did not affect anticholinergic potency consistently. Introduction of Cl into position R1 of the piperazinyl dibenzo-epines, however, removed cataleptogenic and apomorphine-antagonistic properties. Replacement of the Me group in the piperazinyl side-chain of clozapine by a hydroxyethyl or hydroxypropyl group had no effect on the ability to increase striatal dopamine concentration Replacement of H by Cl or F at R2 in clozapine gave derivs. with extrapyramidal effects and which did not increase striatal dopamine content.

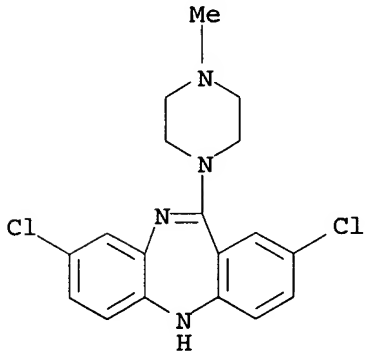
IT **64604-04-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(psychotropic activity of)

RN 64604-04-2 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-2-fluoro-11-(4-methyl-1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **64604-03-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(psychrotropic activity of)
RN 64604-03-1 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L32 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:406038 CAPLUS
DOCUMENT NUMBER: 87:6038
TITLE: Benzazepine derivatives
INVENTOR(S): Schneider, Josef
PATENT ASSIGNEE(S): Dr. A. Wander, A.-G., Switz.
SOURCE: Patentschrift (Switz.), 5 pp.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

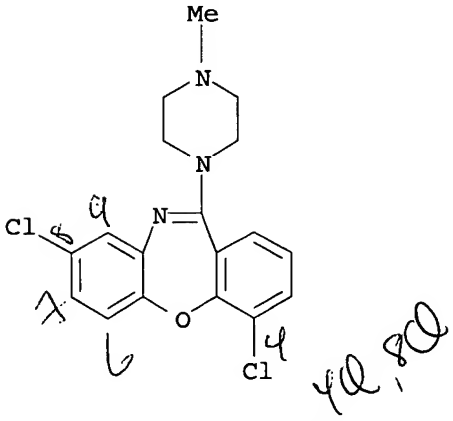
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 585222	A	19770228	CH 1973-2082	19730214
PRIORITY APPLN. INFO.:			CH 1973-2082 A	19730214

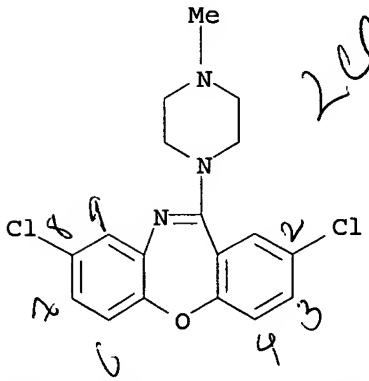
AB I, II and 18 analogs are prepared from piperazine derivs. and thienobenzazepinones or dibenzoxazepinones. Thus, reaction of piperazine with 8-chloro-4,5-dihydro-10H-thieno[3,2-c][1]benzazepin-4-one in PhMe-PhOMe in presence of TiCl4 gives after 3 hr at reflux I.

IT **3455-09-2P 3526-12-3P 19005-32-4P**
19005-36-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

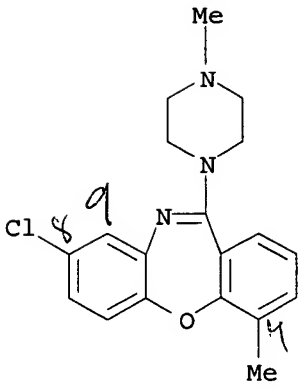
RN 3455-09-2 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 4,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



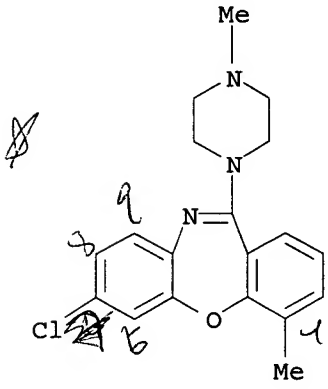
RN 3526-12-3 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 19005-32-4 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 8-chloro-4-methyl-11-(4-methyl-1-piperazinyl)- (8CI, 9CI) (CA INDEX NAME)



RN 19005-36-8 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 7-chloro-4-methyl-11-(4-methyl-1-piperazinyl)-
(8CI, 9CI) (CA INDEX NAME)



L32 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1975:4329 CAPLUS
DOCUMENT NUMBER: 82:4329
TITLE: 11-(1-Piperazinyl)-5H-dibenzo[b,e][1,4]diazepines
INVENTOR(S): Hunziker, Fritz
PATENT ASSIGNEE(S): Dr. A. Wander, A.-G.
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
DE 2413610	A1	19741010	DE 1974-2413610		19740321
NL 7403657	A	19740925	NL 1974-3657		19740319
DD 110498	C	19741220	DD 1974-177349		19740321
BE 812742	A1	19740923	BE 1974-142382		19740322
JP 49126691	A2	19741204	JP 1974-31612		19740322
AU 7467043	A1	19750925	AU 1974-67043		19740322
ZA 7401884	A	19751126	ZA 1974-1884		19740322
FR 2222102	A1	19741018	FR 1974-10147		19740325
PRIORITY APPLN. INFO.:			CH 1973-4259	A	19730323
			CH 1973-5147	A	19730410
			CH 1973-6644	A	19730510

AB Twenty-three dibenzodiazepines I [Rn = 2,4-, 2,7-, 2,8-, 3,7-, 3,8-, or 7,8-Cl2, 2,8-MeCl, -ClBr, -ClMe, -Cl(MeO), or -Cl(MeS), 8,2-Cl(Me2NSO2), or 7,8-(MeO)2, -OCH2O, or -OCH2CH2O; R1 = H or Me; R2 = H, Me, or CH2CH2OH] or their salts were prepared and useful as neuroleptics and (or) antidepressants. Thus, N-methylpiperazine (II) reacted with 2,8-dichloro-10,11-dihydro-5H-dibenzo[b,e][1,4]diazepin-11-one (III) in PhOMe containing TiCl4 to give I (Rn = 2,8-Cl2, R1 = H, R2 = Me), which was also prepared from II and the thioxo analog of III or by methylation of I (Rn = 2,8-Cl2, R1 = R2 = H).

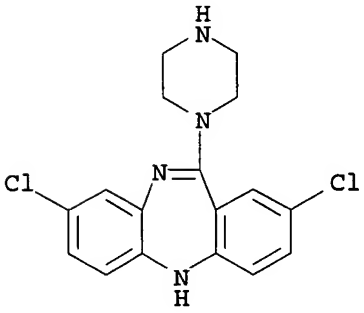
IT **55051-45-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of)

RN 55051-45-1 CAPLUS

CN 5H-Dibenzo[b,e][1,4]diazepine, 2,8-dichloro-11-(1-piperazinyl)-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

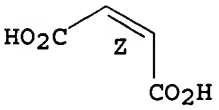
CRN 55051-44-0
CMF C17 H16 Cl2 N4



CM 2

CRN 110-16-7
CMF C4 H4 O4

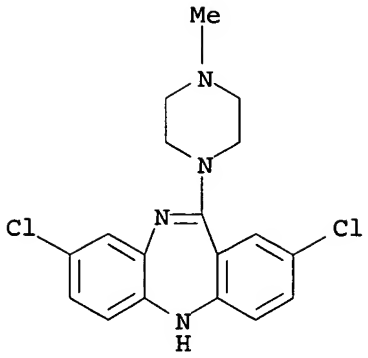
Double bond geometry as shown.



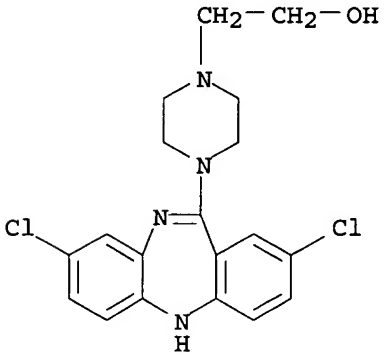
IT **55051-40-6P 55051-46-2P 55051-51-9P**
55051-52-0P 55051-53-1P 55051-54-2P
55051-56-4P 55051-57-5P 55051-58-6P
55051-62-2P 55095-66-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 55051-40-6 CAPLUS

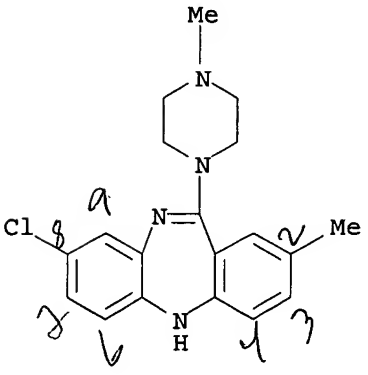
CN 5H-Dibenzo[b,e][1,4]diazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



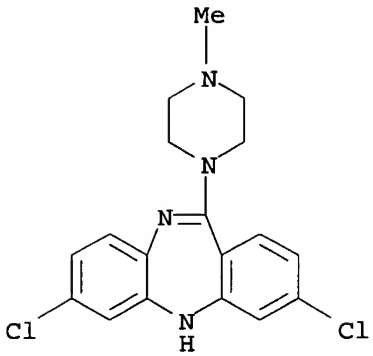
RN 55051-46-2 CAPLUS
CN 1-Piperazineethanol, 4-(2,8-dichloro-5H-dibenzo[b,e][1,4]diazepin-11-yl)-
(9CI) (CA INDEX NAME)



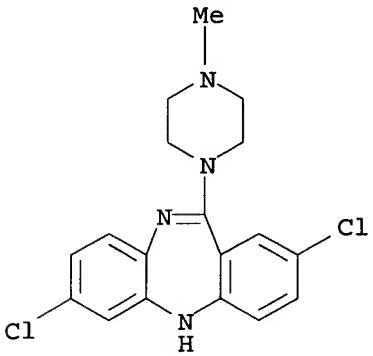
RN 55051-51-9 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-2-methyl-11-(4-methyl-1-
piperazinyl)- (9CI) (CA INDEX NAME)



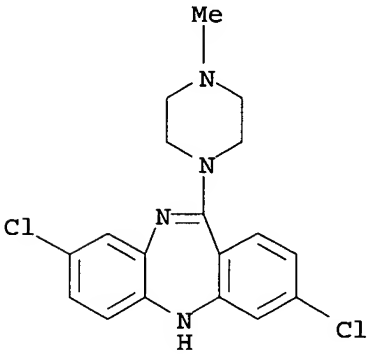
RN 55051-52-0 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 3,7-dichloro-11-(4-methyl-1-piperazinyl)-
(9CI) (CA INDEX NAME)



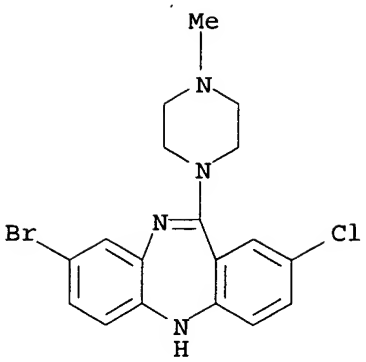
RN 55051-53-1 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 2,7-dichloro-11-(4-methyl-1-piperazinyl)-
(9CI) (CA INDEX NAME)



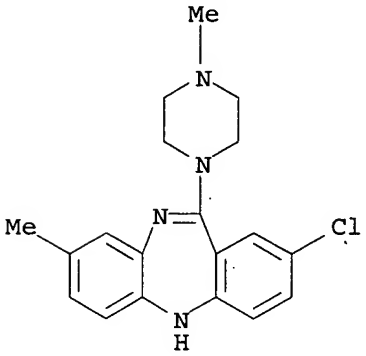
RN 55051-54-2 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 3,8-dichloro-11-(4-methyl-1-piperazinyl)-
(9CI) (CA INDEX NAME)



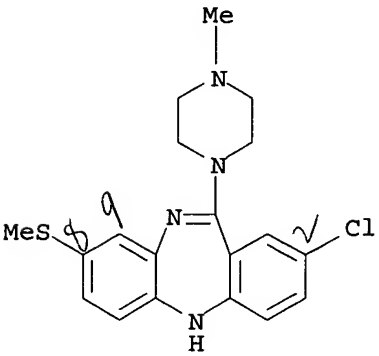
RN 55051-56-4 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-bromo-2-chloro-11-(4-methyl-1-
piperazinyl)- (9CI) (CA INDEX NAME)



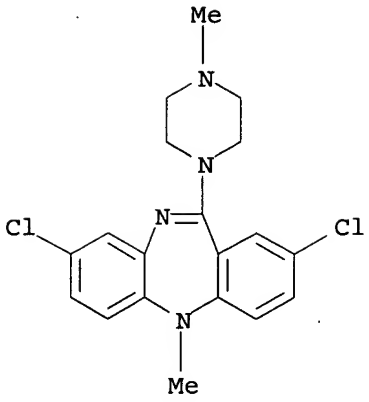
RN 55051-57-5 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 2-chloro-8-methyl-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



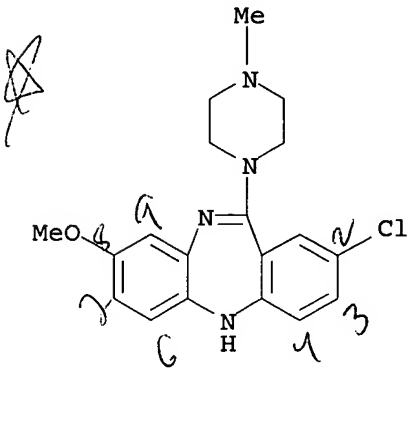
RN 55051-58-6 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 2-chloro-11-(4-methyl-1-piperazinyl)-8-(methylthio)- (9CI) (CA INDEX NAME)



RN 55051-62-2 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 2,8-dichloro-5-methyl-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 55095-66-4 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 2-chloro-8-methoxy-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L32 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1974:14969 CAPLUS
DOCUMENT NUMBER: 80:14969
TITLE: Piperazinyl-substituted dibenzoxazepines and similar compounds
INVENTOR(S): Schneider, Josef
PATENT ASSIGNEE(S): Wander A.-G.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

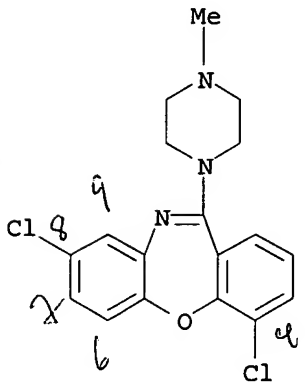
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2316438	A1	19731011	DE 1973-2316438	19730402
DE 2316438	B2	19760616		
DE 2316438	C3	19770127		
CH 569730	A	19751128	CH 1972-4898	19720404
CH 569731	A	19751128	CH 1972-4901	19720404
JP 49013189	A2	19740205	JP 1973-11246	19730129
DK 150850	B	19870706	DK 1973-1652	19730326
DK 150850	C	19871130		
NO 138210	C	19780726	NO 1973-1257	19730327
FI 61029	B	19820129	FI 1973-943	19730327
FI 61029	C	19820510		

SU 457220	D	19750115	SU 1973-1900401		19730329
NL 7304441	A	19731008	NL 1973-4441		19730330
NL 175621	B	19840702			
NL 175621	C	19841203			
BE 797671	A1	19731002	BE 1973-129561		19730402
GB 1418363	A	19751217	GB 1973-15667		19730402
ES 413252	A1	19760501	ES 1973-413252		19730402
PL 89178	P	19761030	PL 1973-161672		19730402
CS 178125	P	19770831	CS 1973-2346		19730402
RO 72458	P	19810228	RO 1973-74359		19730402
JP 49013190	A2	19740205	JP 1973-37479		19730403
JP 51042118	B4	19761113			
DD 105614	C	19740512	DD 1973-169911		19730403
HU 166524	P	19750328	HU 1973-WA277		19730403
AT 7302911	A	19770415	AT 1973-2911		19730403
AT 340428	B	19771212			
FR 2179071	A1	19731116	FR 1973-12056		19730404
ZA 7302347	A	19741127	ZA 1973-2347		19730404
US 3962248	A	19760608	US 1975-553142		19750226
PRIORITY APPLN. INFO.:			CH 1972-4898	A	19720404
			CH 1972-4901	A	19720404
			US 1973-346343	A1	19730329

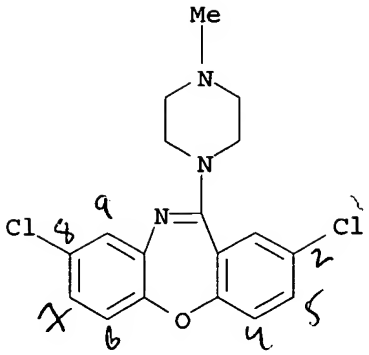
AB About 40 piperazines (I, X = CH2, NH, NMe, S, or O; R = e.g. H, C1-4 alkyl, CH2CH2OH, or CH2CH2O2CBu; R1 = e.g. H, 2-Cl, 2-NO2, 2-COMe, 2-SMe, 2-SO2CF3, 2-SCF3, or 1-Me; R2 = H or Me; R3 = H, Me, or Cl; R4 = H or 7- or 8-Cl; and II, R5 = H, 7-Me, or 7- or 8-Cl) or their hydrochlorides, maleates, or fumarates were prepared by reaction of corresponding carbonyl compds., e.g. III, with 1-R-substituted piperazines. Thus, N-methylpiperazine was treated successively with TiCl4 in PhMe and PhOMe at 50-5° and with III at reflux to give 90% I (X = NH, R = Me, R1 = R2 = R3 = H, R4 = 8-Cl).

IT **3455-09-2P 3526-12-3P 19005-32-4P 19005-36-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

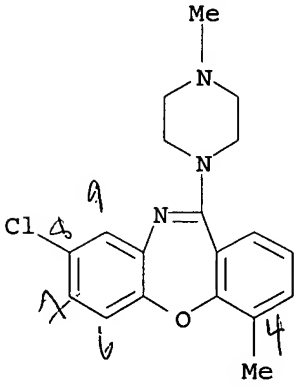
RN 3455-09-2 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 4,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



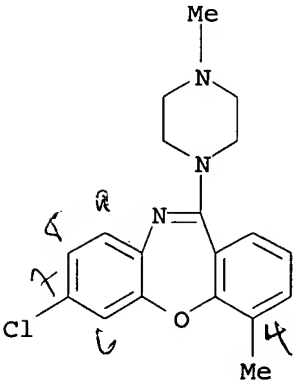
RN 3526-12-3 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 19005-32-4 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 8-chloro-4-methyl-11-(4-methyl-1-piperazinyl)-(8CI, 9CI) (CA INDEX NAME)



RN 19005-36-8 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 7-chloro-4-methyl-11-(4-methyl-1-piperazinyl)-(8CI, 9CI) (CA INDEX NAME)



L32 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:427466 CAPLUS
DOCUMENT NUMBER: 69:27466
TITLE: Substituted dibenz[b,f][1,4]oxazepines
INVENTOR(S): Schmutz, Jean; Hunziker, Fritz; Kuenzle, Franz M.
PATENT ASSIGNEE(S): Dr. A. Wander, A.-G.
SOURCE: Patentschrift (Switz.), 3 pp.

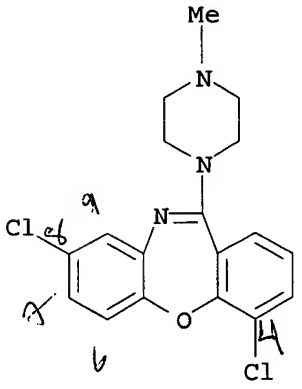
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 436297		19671115	CH	19640527

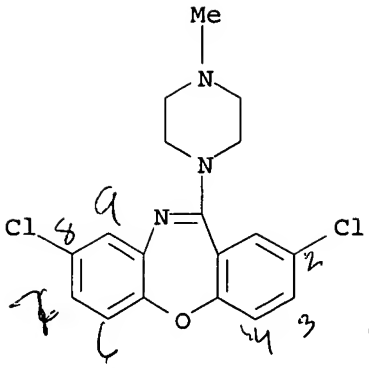
AB 11-(4-Methyl-1-piperazinyl)dibenz[b,f] [1,4]-oxazepines (I) were prepared by methylating the corresponding 11-(1-piperazinyl) dibenz [b,f] [1,4]oxazepine. Thus, 6.26 g. 2-chloro-11-(1-piperazinyl) dibenz [b,f] [1,4]oxazepine in 50 ml. C6H6 at 60° was treated with 1.42 g. MeI and 30 ml. C6H6 and refluxed for 30 min. to give 2.7 g. I (R = H, R' = 2-Cl), m. 109-10°. The following I were similarly prepared (R, R', and m.p. given): H, H, 97-8°; 7-Cl, H, 147-8°; 8-Cl, 2-Cl, 130-1°; 8-Cl, 4-Cl, 134-5°; H, 4-Me, 179-82°; H, 2-Me, 130-1°; H, 4-Cl, 173-4°; 6-Cl, H, 83-7°; H, 3-Me, 103-5°; H, 2-Br, 95-9°; H, 3,4-Me2, 167-8°; H, 2-F, 81-6°; H, 1,4-Me2, 143-4°; H, 3-Cl, 122-4°; 8-Cl, 4-Me, 151-2°; H, 2-OMe, 107-8°; H, 4-Et, 128-30°; H, 2,4-Cl2, 135-8°; 7-Cl, 4-Me, 167-8°. 11-(4-Hydroxyethyl-1-piperazinyl)- and 11-(4-acetoxyethyl-1-piperazinyl)dibenz[b,f] [1,4]oxazepine-2HCl, m. 197-237° and 155-60°, resp., were also prepared I are neuroplegics, neuroleptics, and analgesics. The following oral LD50 and ED50 in the motility damping test in mice were found (R, R', LD50 mg./kg., ED50 mg./kg. given): H, H, 230, 2.7; H, 2-Cl, 47, 0.05; H, 2-Br, 95, 0.05; H, 2-F, 120, 0.13; H, 4-Cl, 800, 5.4; 8-Cl, H, 410, 10.5; (chlorpromazine, 135, 3.5).

IT **3455-09-2P 3526-12-3P 19005-32-4P 19005-36-8P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(manufacture and pharmacology of)

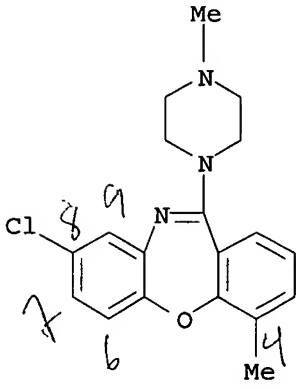
RN 3455-09-2 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 4,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



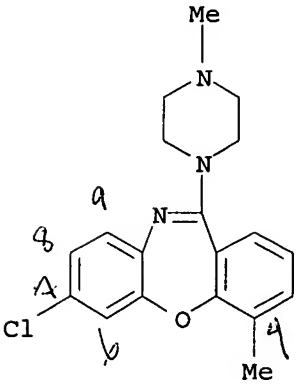
RN 3526-12-3 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 19005-32-4 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 8-chloro-4-methyl-11-(4-methyl-1-piperazinyl)-(8CI, 9CI) (CA INDEX NAME)



RN 19005-36-8 CAPLUS
CN Dibenz[b,f][1,4]oxazepine, 7-chloro-4-methyl-11-(4-methyl-1-piperazinyl)-(8CI, 9CI) (CA INDEX NAME)



L32 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:463200 CAPLUS
DOCUMENT NUMBER: 63:63200
ORIGINAL REFERENCE NO.: 63:11592g-h,11593a-c
TITLE: 11-Substituted dibenz[b,f][1,4]oxazepines
PATENT ASSIGNEE(S): Dr. A. Wander A.-G
SOURCE: 13 pp.

DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6406089	A	19641201	NL 1964-6089	19640529
SE 321664	B	19700316	SE 1961-8266	19610816
SE 335857	B	19710614	SE 1965-7028	19610816
SE 336801	B	19710719	SE 1967-2711	19630514
SE 300111	B	19680408	SE 1965-12187	19640522
SE 317382	B	19691117	SE 1965-12185	19640522
DE 1470426	A	19691218	DE 1964-W36859	19640525
DE 1470426	B2	19790315		
DE 1470426	C3	19791108		
NO 115657	B	19681111	NO 1964-153434	19640528
FI 42214	B	19700302	FI 1964-1159	19640528
NL 6413698	A	19650125	NL 1964-13698	19641125
DK 118463	B	19700824	DK 1965-1458	19650322
DE 1720007	A	19710519	DE 1968-W45792	19680304
IL 29571	A1	19720427	IL 1968-29571	19680304
GB 1216523	A	19701223	GB 1968-1216523	19680305
AT 292707	B	19710910	AT 1968-2153	19680305
AT 292716	B	19710910	AT 1970-204	19680305
AT 292717	B	19710910	AT 1970-205	19680305
AT 292718	B	19710910	AT 1970-206	19680305
AT 292719	B	19710910	AT 1970-207	19680305
AT 292720	B	19710910	AT 1970-208	19680305
AT 292721	B	19710910	AT 1970-209	19680305
AT 292722	B	19710910	AT 1970-210	19680305
ES 351389	A1	19691201	ES 1968-351389	19680308
SE 364277	B	19740218	SE 1968-3129	19680308
FR 8046	M	19700810	FR 1968-8046	19680312
NO 123459	B	19711122	NO 1968-946	19680312
JP 48034599	B4	19731022	JP 1968-15666	19680312
BE 712114	A	19680913	BE 1968-712114	19680313
NL 6803570	A	19680916	NL 1968-3570	19680313
US 3539573	A	19701110	US 1968-769373	19681021
US 3908010	A	19750923	US 1974-435430	19740122

PRIORITY APPLN. INFO.:

CH 1963-6762	A	19630530
CH 1963-11907	A	19630927
CH 1960-9276	A	19600816
CH 1960-13542	A	19601202
CH 1961-8529	A	19610720
CH 1962-6350	A	19620525
CH 1962-14251	A	19621205
CH 1962-14252	A	19621205
CH 1962-14253	A	19621205
CH 1963-1902	A	19630215
CH 1967-3582	A	19670313
CH 1967-4103	A	19670322
CH 1967-6557	A	19670509
CH 1967-10115	A	19670714
CH 1967-15453	A	19671103
US 1968-769373	A2	19681021
US 1970-57317	A1	19700722

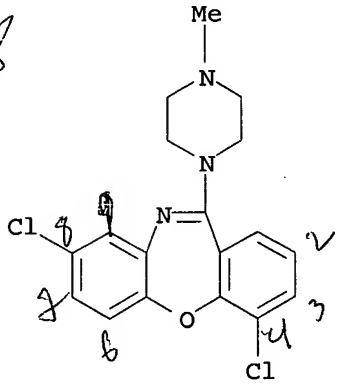
AB I were prepared in 3 ways (Method a). A mixture of 10 g. 2-chloro-10,11-dihydro-11-oxodibenz[b,f][1,4]oxazepine, 3 ml. N,N-dimethylaniline, and 80 ml. POCl3 was refluxed 3 hrs. to give 9.3 g. 2,11-dichlorodibenz[b,f][1,4]oxazepine (II), m. 131-4°. II (9.3 g.) in 100 ml. xylene was refluxed 4 hrs. with 10 ml. N-methylpiperazine to give 8.9 g. 2-chloro-11-(4-methyl-1-piperazinyl)dibenz[b,f] [1,4]oxazepine, m. 109-10°. Similarly, a mixture of 8 g. 8-chloro-10,11-dihydro-11-

oxodibenz[b,f][1,4]oxazepine, 8 g. PCl5, and 50 ml. POCl3 was refluxed 4 hrs. and the crude product treated with 10 ml. N-methylpiperazine to give 5.9 g. 8-chloro-11-(4-methyl-1-piperazinyl)dibenz[b,f] [1,4] oxazepine, m. 165-6°. (Method b). 2-[(4-Methyl-1-piperazinyl)carboxamido]phenyl Ph ether (13.4 g.) was refluxed 30 hrs. with 150 ml. POCl3 to give 6.2 g. 11-(4-methyl-1-piperazinyl)dibenz[b,f][1,4]oxazepine (III), m. 97-8°. (Method c). 2-Aminodiphenyl ether 2'-thiocarboxylic acid 4-methylpiperazide (8.3 g.) with 8.5 g. powdered mercuric acetate in 10 ml. xylene was refluxed 24 hrs. to give 4.5 g. III. The general procedures illustrated above were used to prepare the following I (11-substituent, other substituent(s), and m.p. given): NH(CH2)3NMe2, --, 109°; NH(CH2)2NMe2, --, 88-9°; 4-methylpiperazin-1-yl, 7-Cl, 147-8°; 4-methylpiperazin-1-yl,2,8-dichloro, 130-1°; 4-methylpiperazin-1-yl, 4,8-dichloro, 134-5°; NH(CH2)2NEt2, 4-Me, 43-5°; 4-methylpiperazin-1-yl, 4-Me, 179-82°; 4-methylpiperazin-1-yl, 2-Me, 130-1°; 4-methylpiperazin-1-yl, 4-Cl, 173-4°; NH(CH2)2NEt2, 4-Cl, 96-7°; 4-methylpiperazine, 6-Cl, 83-7°; 4-methylpiperazin-1-yl, 3-Me, 103-5°; 4-methylpiperazin-1-yl, 2-Br, 95-9°; 4-methylpiperazin-1-yl, 3,4-dimethyl, 167-8°; 4-methylpiperazin-1-yl, 2-F, 84-6°; 4-methylpiperazin-1-yl, 1,4-dimethyl, 143-4°; 4-methylpiperazin-1-yl, 3-Cl, 122-4°; NH(CH2)3NMe2, 4-Me, 126-7°; NMe(CH2)3NMe2, 4-Me, 201-3° (di-HCl salt); 4-(2-hydroxyethyl) piperazin-1-yl, 2-Cl, 197-237° (diHCl salt); NHCHMe(CH2)3NEt2, 4-Me,-- (b0.05 200-10°); NH(CH2)2NH2, --, 133-5°. I show neurological and analgesic properties.

IT **3455-09-2**, Dibenz[b,f][1,4]oxazepine, 4,8-dichloro-11-(4-methyl-1-piperazinyl)- **3526-12-3**, Dibenz[b,f][1,4]oxazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)-
(preparation of)

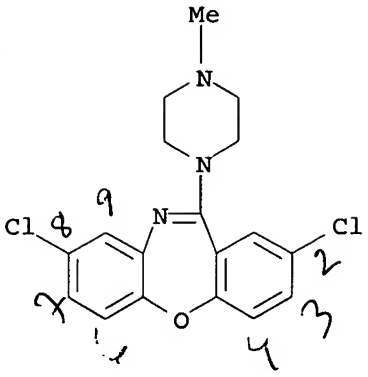
RN 3455-09-2 CAPLUS

CN Dibenz[b,f][1,4]oxazepine, 4,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 3526-12-3 CAPLUS

CN Dibenz[b,f][1,4]oxazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



L32 ANSWER 19 OF 26 USPATFULL on STN

ACCESSION NUMBER: 2005:234355 USPATFULL

TITLE: Piperazine substituted aryl benzodiazepines and their use as dopamine receptor antagonists for the treatment of psychotic disorders

INVENTOR(S): Aicher, Thomas Daniel, Superior, CO, UNITED STATES
Chen, Zhaogen, Noblesville, IN, UNITED STATES
Krushinski, Joseph Herman Jr, Brownsburg, IN, UNITED STATES
Le Huerou, Yvan, Boulder, CO, UNITED STATES
Pineiro-Nunez, Marta Maria, Brownsburg, IN, UNITED STATES
Ruley, Kevin Michael, Indianapolis, IN, UNITED STATES
Schaus, John Mehnert, Zionsville, IN, UNITED STATES
Thompson, Dennis Charles, Indianapolis, IN, UNITED STATES
Tupper, David Edward, Reading, UNITED KINGDOM
Chen, Ying, Thousand Oaks, CA, UNITED STATES
Faul, Margaret Mary, Zionsville, IN, UNITED STATES
Rocco, Vincent Patrick, Indianapolis, IN, UNITED STATES

PATENT ASSIGNEE(S): Eli Lilly and Company (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005203296	A1	20050915	
APPLICATION INFO.:	US 2003-505805	A1	20030317	(10)
	WO 2003-US6708		20030317	
			20040826	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-368670P	20020328 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: ELI LILLY AND COMPANY, PATENT DIVISION, P.O. BOX 6288, INDIANAPOLIS, IN, 46206-6288, US

NUMBER OF CLAIMS: 56

EXEMPLARY CLAIM: 1

LINE COUNT: 8339

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described herein are antipyschotic compounds of formula (I) wherein, A is an optionally benzo-fused five or six member aromatic ring having zero to three hetero atoms independently selected from N, O, and S; Alk is (C.sub.1-4) alkylene optionally substituted with OH, methoxy, ethoxy, or F; Ar is optionally substituted phenyl, naphthyl, monocyclic heteroaromatic, or bicyclic heteroaromatic; R.sup.1 is hydrogen or (C.sub.1-4) alkyl optionally substituted with OH, OR.sup.3, or OCH.sub.2CH.sub.2OH, wherein R.sup.3 is (C.sub.1-2) alkyl; R.sup.2 is H, (C.sub.1-6) alkyl, halogen, fluorinated (C.sub.1-6) alkyl, OR.sup.4,

SR.sup.4, NO.sub.2, CN, COR.sup.4, CONR.sup.5R.sup.6, SO.sub.2NR.sup.5R.sup.6, NR.sup.5R.sup.6, NR.sup.5COR.sup.4, NR.sup.5SO.sub.2R.sup.4, or optionally substituted phenyl, wherein R.sup.4 is hydrogen, (C.sub.1-6) alkyl, fluorinated (C.sub.1-6) alkyl, benzyl, or optionally substituted phenyl, R.sup.5 and R.sup.6 are independently hydrogen, (C.sub.1-6) alkyl, or optionally substituted phenyl; Z is one or two substituents independently selected from hydrogen, halogen, (C.sub.1-6) alkyl, fluorinated (C.sub.1-6) alkyl, OR.sup.7, SR.sup.7, NO.sub.2, CN, COR.sup.7, CONR.sup.8R.sup.9, SO.sub.2NR.sup.8R.sup.9, NR.sup.8SO.sub.2R.sup.7, NR.sup.8R.sup.9, or optionally substituted phenyl, wherein R.sup.7 is hydrogen, (C.sub.1-6) alkyl, fluorinated alkyl, benzyl, or optionally substituted phenyl, R.sup.8 and R.sup.9 are independently hydrogen, (C.sub.1-6) alkyl, or optionally substituted phenyl; and salts, solvates, and crystal forms thereof. Also described are the use of the compounds of formula (a) as antagonists of the dopamine D.sub.2 receptor and as agents for the treatment of psychosis and bipolar disorders, and pharmaceutical formulations of the compounds of formula (I). Also described are compounds useful as intermediates for the synthesis of the compounds of formula (I). ##STR1##

IT **612506-11-3P 612506-13-5P 612506-15-7P 612506-17-9P**
(antipsychotic; preparation of aryl-fused benzodiazepine D2 receptor antagonists as antipsychotics)

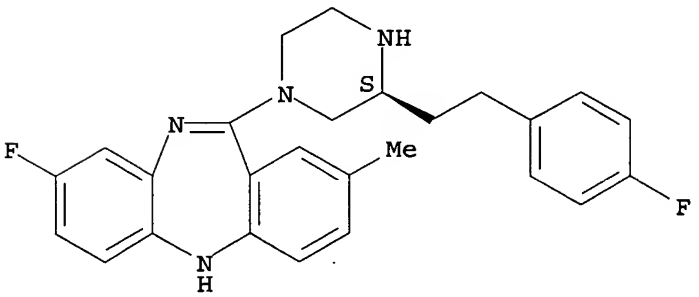
RN 612506-11-3 USPATFULL

CN Butanedioic acid, compd. with 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-1-piperazinyl]-2-methyl-5H-dibenzo[b,e][1,4]diazepine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 612506-10-2
CMF C26 H26 F2 N4

Absolute stereochemistry.



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

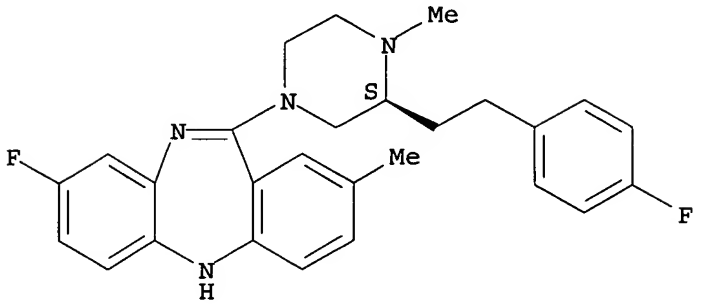
RN 612506-13-5 USPATFULL

CN Butanedioic acid, compd. with 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-4-methyl-1-piperazinyl]-2-methyl-5H-dibenzo[b,e][1,4]diazepine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 612506-12-4
CMF C27 H28 F2 N4

Absolute stereochemistry.



CM 2

CRN 110-15-6
CMF C4 H6 O4

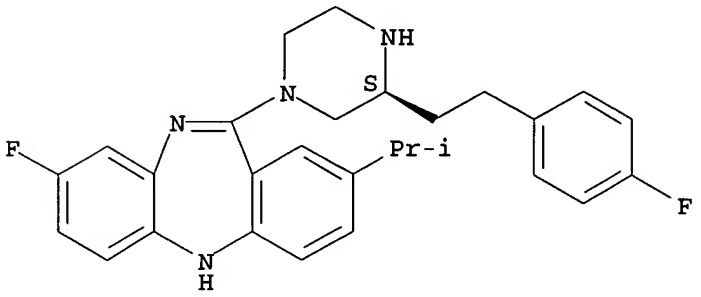
$HO_2C-CH_2-CH_2-CO_2H$

RN 612506-15-7 USPATFULL
CN Butanedioic acid, compd. with 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-1-piperazinyl]-2-(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 612506-14-6
CMF C28 H30 F2 N4

Absolute stereochemistry.



CM 2

CRN 110-15-6
CMF C4 H6 O4

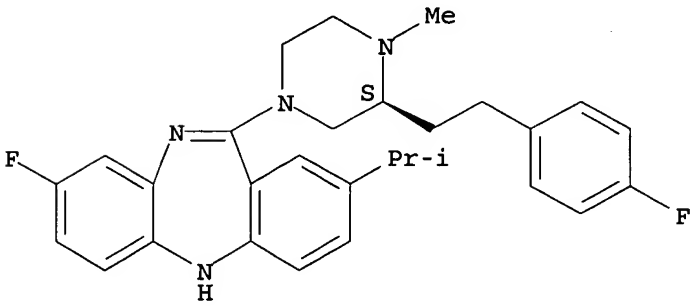
$HO_2C-CH_2-CH_2-CO_2H$

RN 612506-17-9 USPATFULL
CN Butanedioic acid, compd. with 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-4-methyl-1-piperazinyl]-2-(1-methylethyl)-5H-dibenzo[b,e][1,4]diazepine (1:1) (9CI) (CA INDEX NAME)

CM 1

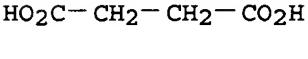
CRN 612506-16-8
CMF C29 H32 F2 N4

Absolute stereochemistry.



CM 2

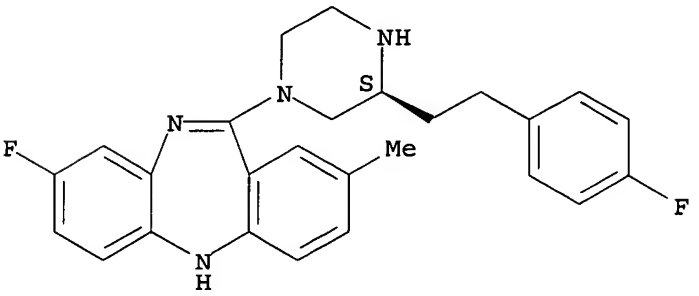
CRN 110-15-6
CMF C4 H6 O4



IT **612506-10-2P 612506-12-4P 612506-14-6P 612506-16-8P**
(intermediate; preparation of aryl-fused benzodiazepine D2 receptor antagonists as antipsychotics)

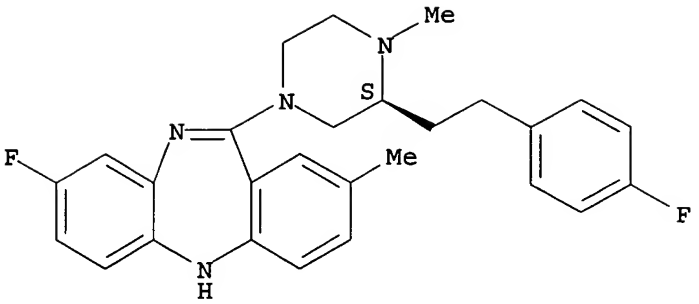
RN 612506-10-2 USPATFULL
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-1-piperazinyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



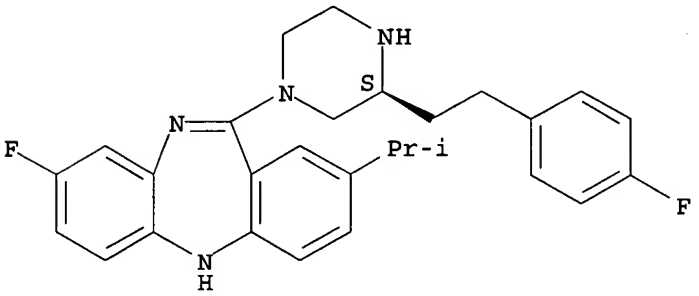
RN 612506-12-4 USPATFULL
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-4-methyl-1-piperazinyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



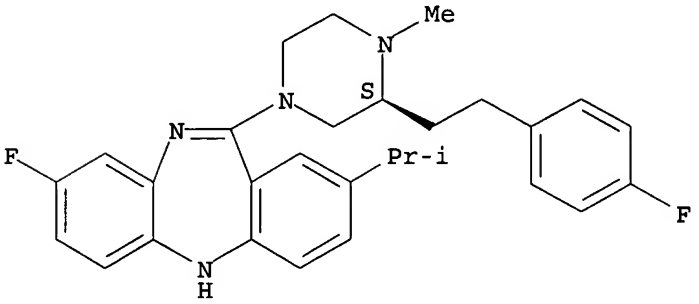
RN 612506-14-6 USPATFULL
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-1-piperazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 612506-16-8 USPATFULL
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-fluoro-11-[(3S)-3-[2-(4-fluorophenyl)ethyl]-4-methyl-1-piperazinyl]-2-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L32 ANSWER 24 OF 26 USPATFULL on STN
ACCESSION NUMBER: 97:120266 USPATFULL
TITLE: N-methyl piperazine compounds having dopamine receptor affinity
INVENTOR(S): Fu, Jian-Min, Brampton, Canada
Rakhit, Sumanas, Mississauga, Canada
PATENT ASSIGNEE(S): Allelix Biopharmaceuticals, Inc., Mississauga, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5700445		19971223
APPLICATION INFO.:	US 1994-354905		19941212 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Kight, John		
ASSISTANT EXAMINER:	Jones, Dameron		
LEGAL REPRESENTATIVE:	Nikaido, Marmelstein, Murray & Oram LLP		
NUMBER OF CLAIMS:	9		
EXEMPLARY CLAIM:	1		
LINE COUNT:	671		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described herein are D4 receptor-selective compounds of the general formula: ##STR1## wherein X.sub.1 is selected from CH.sub.2, NH, O and S;

X.sub.2 - - is selected from CH.dbd., CH.sub.2 13 , and N.dbd.;

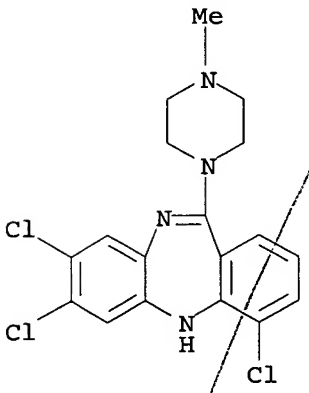
R.sub.1 to R.sub.8 are each independently selected from H, C.sub.1-4 alkyl, halo, cyano, nitro and halo-substituted C.sub.1-4 alkyl

and acid addition salts, solvates and hydrates thereof. Their use as ligands for dopamine receptor identification and in a drug screening program, and as pharmaceuticals to treat indications in which the D4 receptor is implicated, such as schizophrenia, is also described.

IT **179385-70-7P 179385-75-2P**
((piperazinyl)dibenzo[b,e][1,4]diazepines and (piperazinyl)dibenzo[b,f]thiepins as dopaminergic neurotransmitter agonists or antagonists)

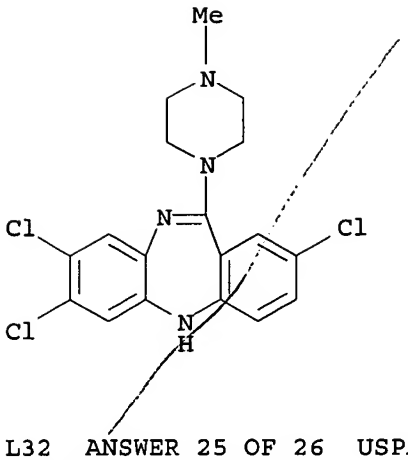
RN 179385-70-7 USPATFULL

CN 5H-Dibenzo[b,e][1,4]diazepine, 4,7,8-trichloro-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 179385-75-2 USPATFULL

CN 5H-Dibenzo[b,e][1,4]diazepine, 2,7,8-trichloro-11-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L32 ANSWER 25 OF 26 USPATFULL on STN

ACCESSION NUMBER:	96:65556 USPATFULL
TITLE:	Dopamine receptor ligands
INVENTOR(S):	Tehim, Ashok, Mississauga, Canada Fu, Jian-Min, Brampton, Canada Rakhit, Sumanas, Mississauga, Canada
PATENT ASSIGNEE(S):	Allelix Biopharmaceuticals Inc., Mississauga, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5538965		19960723
APPLICATION INFO.:	US 1994-355297		19941212 (8)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-172208, filed on 23 Dec 1993, now abandoned
DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Datlow, Philip I.
LEGAL REPRESENTATIVE:	Foley & Lardner
NUMBER OF CLAIMS:	29
EXEMPLARY CLAIM:	1
LINE COUNT:	1206

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described herein are D4 receptor-selective compounds of the general formula: ##STR1## wherein: A and B are independently selected, optionally substituted, saturated or unsaturated 5- or 6-membered, homo- or heterocyclic rings;

X.sub.1 is selected from CH.sub.2, O, NH, S, C.dbd.O, CH--OH, CH--N(C.sub.1-4 alkyl).sub.2, C.dbd.CHCl, C.dbd.CHCN, N-C.sub.1-4 alkyl, N-acetyl, SO.sub.2 and SO;

X.sub.2 -- is selected from N.dbd., CH.sub.2 --, CH.dbd., C(O)--, O--, and S--;

R.sub.1 represents C.sub.1-4 alkyl;

Y is selected from CH and N;

n is 0, 1 or 2;

q is 1 or 2;

R.sub.2 is C.sub.1-6 alkyl optionally incorporating a heteroatom selected from N, O and S;

D is cyclohexane or benzene; and

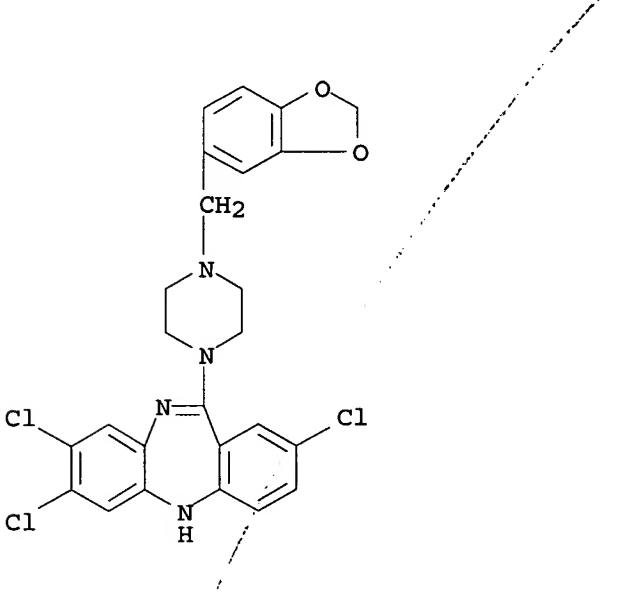
E is a saturated or unsaturated 5- or 6-membered heterocycle incorporating 1, 2 or 3 heteroatoms selected from O, N, and S, wherein E is optionally substituted with 1 or 2 substituents selected from halogen, C.sub.1-4 alkyl and halogen-substituted C.sub.1-4 alkyl;

and acid addition salts, solvates and hydrates thereof. Their use as ligands for dopamine receptor identification and in a drug screening program, and as pharmaceuticals to treat indications in which the D4 receptor is implicated, such as schizophrenia, is also described.

IT **167996-86-3P**
(dopamine receptor ligands)

RN 167996-86-3 USPATFULL

CN 5H-Dibenzo[b,e][1,4]diazepine, 11-[4-(1,3-benzodioxol-5-ylmethyl)-1-piperazinyl]-2,7,8-trichloro- (9CI) (CA INDEX NAME)



L32 ANSWER 26 OF 26 USPATFULL on STN

ACCESSION NUMBER:	76:32142 USPATFULL
TITLE:	Process for making 11-piperazino-diazepines, oxazepines, thiazepines and azepines
INVENTOR(S):	Schneider, Josef, Minusio, Switzerland
PATENT ASSIGNEE(S):	Sandoz, Inc., Hanover, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3962248		19760608
APPLICATION INFO.:	US 1975-553142		19750226 (5)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1973-346343, filed on 29 Mar 1973, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	CH 1972-4898	19720404
	CH 1972-4901	19720404

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Rollins, Alton D.
ASSISTANT EXAMINER:	Tovar, Jose
LEGAL REPRESENTATIVE:	Sharkin, Gerald D., Honor, Robert S., McGovern, Thomas O.
NUMBER OF CLAIMS:	8
EXEMPLARY CLAIM:	1
LINE COUNT:	528

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention concerns a novel process for the preparation of 6-piperazinyl derivatives of morphantridine and corresponding ring-substituted and hereto analogues thereof, comprising reacting a compound of the formula: ##SPC1##

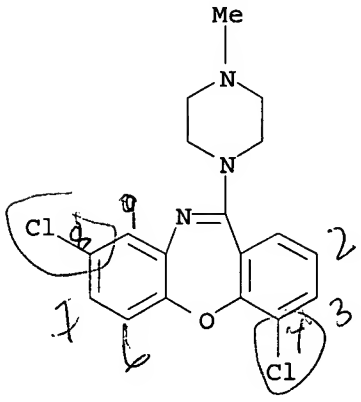
Wherein A is benzene or thiophene, and X is --CH.sub.2 -- or a hetero atom or group, with a complex comprising titanium, zirconium, hafnium or vanadium and a corresponding piperazinyl derivative.

The end products are in general known and useful as neuroleptics.

IT **3455-09-2P 3526-12-3P 19005-32-4P**
19005-36-8P
(preparation of)

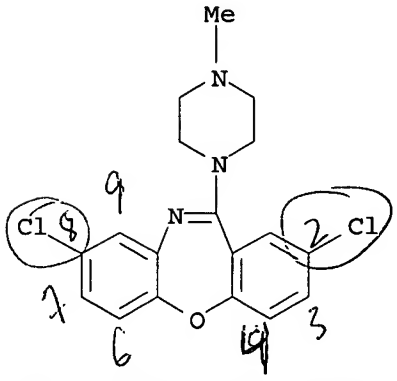
RN 3455-09-2 USPATFULL

CN Dibenz[b,f][1,4]oxazepine, 4,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



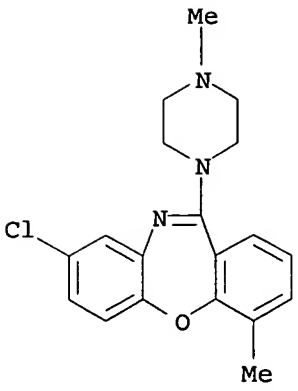
RN 3526-12-3 USPATFULL

CN Dibenz[b,f][1,4]oxazepine, 2,8-dichloro-11-(4-methyl-1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

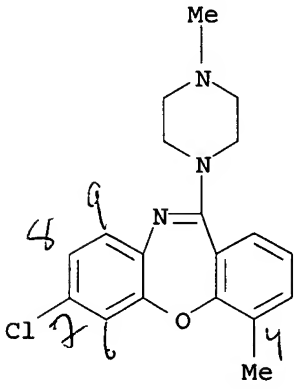


RN 19005-32-4 USPATFULL

CN Dibenz[b,f][1,4]oxazepine, 8-chloro-4-methyl-11-(4-methyl-1-piperazinyl)- (8CI, 9CI) (CA INDEX NAME)



RN 19005-36-8 USPATFULL
CN Dibenz[b,f][1,4]oxazepine, 7-chloro-4-methyl-11-(4-methyl-1-piperazinyl)-
(8CI, 9CI) (CA INDEX NAME)



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7 Cl 4 me